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Cognitive impairment in PSP compared with PD: assessment by clinical subtype and longitudinal change

Takeharu Tsuboi ,[1] Hiroshi Tatsumi,[2] Kosuke Kobayasi,[1] Rina Hashimoto,[3] Ikuko Aiba[3]

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[1]Department of Rehabilitation, National Hospital Organization Higashinagoya National Hospital, Nagoya, Japan
[2]Aichi Gakuin University, Nissin, Japan
[3]Department of Neurology, National Hospital Organization Higashinagoya National Hospital, Nagoya, Japan

Correspondence to
Takeharu Tsuboi;
tsuboi.takeharu.jh@mail.hosp.go.jp

ABSTRACT

Background Longitudinal studies investigating cognitive function changes in patients with progressive supranuclear palsy (PSP) are limited. The variability of cognitive impairment across clinical subtypes of PSP remains unclear.

Objective This study aimed to compare the longitudinal changes in cognitive function between patients with PSP and Parkinson's disease (PD) and to assess differences in cognitive impairment among PSP subtypes.

Methods A retrospective observational study was conducted using neuropsychological testing data from patients with PSP and PD admitted to our hospital.

Results The study included 38 patients with PD and 41 patients with PSP (23 PSP-Richardson's syndrome, 14 PSP-progressive gait freezing (PSP-PGF), 3 PSP-Parkinsonism and 1 PSP-predominant corticobasal syndrome). At baseline, cognitive function was significantly lower in the PSP group than in the PD group. Over 12 months, patients with PSP exhibited significant declines in multiple cognitive domains, whereas no significant changes were observed in the PD group. Among PSP subtypes, PSP-RS showed a faster rate of cognitive decline than PD, while PSP-PGF demonstrated a lower progression than PSP-RS.

Conclusion PSP is associated with progressive cognitive impairment, with rates of decline varying by subtype. PSP-PGF exhibited a slower progression than PSP-RS. Clinical management should consider subtype-specific differences in cognitive prognosis to tailor treatment and care.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Progressive supranuclear palsy (PSP) is associated with a higher prevalence of cognitive impairment than Parkinson's disease (PD) with pronounced frontal lobe dysfunction.

WHAT THIS STUDY ADDS

⇒ PSP demonstrated progressive cognitive decline over 12 months, while PD showed no significant changes. Among PSP subtypes, PSP-progressive gait freezing had slower cognitive decline than PSP-Richardson's syndrome.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Long-term evaluations of PSP by clinical subtype are essential for optimising patient management and prognosis.

INTRODUCTION

Progressive supranuclear palsy (PSP) is a rare neurodegenerative disorder typically manifesting in middle-aged or older adults. Characterised by early-onset postural instability, PSP presents with symptoms such as supranuclear oculomotor dysfunction, gait disturbances, dysarthria, dysphagia, neck and upper body rigidity and cognitive impairment.[1]

Since a 2005 study using hierarchical cluster analysis of 103 pathologically confirmed PSP cases in the UK, multiple subtypes of PSP have been identified. These include PSP-Parkinsonism (PSP-P),[2] characterised by Parkinsonism; PSP-pure akinesia with gait freezing,[3] marked by gait freezing; and PSP with cerebellar ataxia,[4] defined by significant limb ataxia. The most common clinical presentation, Richardson's syndrome (PSP-RS), primarily features oculomotor dysfunction and severe postural instability.[2] PSP prevalence ranges from 5 to 20 per 100 000 individuals globally.[5]

Cognitive dysfunction in PSP typically involves mild memory deficits and pronounced frontal lobe impairments, such as reduced executive function, verbal fluency and initiation.[6]

Parkinson's disease (PD) is a neurodegenerative disorder characterised by the presence of Lewy bodies and the degeneration and loss of dopaminergic neurons in the substantia nigra. The primary motor symptoms of PD include bradykinesia, resting tremor, muscle rigidity and postural instability.[7] PD is prevalent, affecting approximately 1 in 1000 individuals, making it the second most common neurodegenerative disorder after Alzheimer's disease.[8]

In addition, to motor symptoms, PD is associated with non-motor symptoms, including

psychiatric symptoms (eg, depression and apathy), autonomic dysfunction, olfactory impairment and cognitive deficits. Cognitive dysfunction in PD encompasses impairments in memory and executive function which may manifest during early or even preclinical stages.[9] Among non-motor symptoms, cognitive dysfunction is the most prevalent with dementia observed in 60% of patients 12-year postdiagnosis and 80% of patients 20 years after diagnosis.[10] Early cognitive dysfunction in PD typically spares memory and orientation but is marked by impairments in attention, executive dysfunction and visuospatial cognition.[11]

PSP is a rarer, rapidly progressing neurodegenerative disorder with a poorer prognosis than PD.[12] While studies on cognitive dysfunction in atypical Parkinsonism are limited compared with PD,[13] PSP has been less studied, particularly regarding its longitudinal impact on cognitive function. Few studies have explored differences in cognitive trajectories among PSP clinical subtypes[14 15] and research on Japanese patients remains scarce. Addressing these gaps may enhance the differentiation of PSP from PD and improve patient care.[15]

This study aimed to compare longitudinal changes in cognitive function between patients with PSP and PD and to investigate these changes across PSP clinical subtypes.

METHODS

Research design

This study employed a retrospective observational design.

Research period

Data were collected between 1 April 2013 and 31 August 2023.

Participants

Participants were patients diagnosed with PD or PSP who were admitted to the National Hospital Organization Higashinagoya National Hospital. Cognitive function evaluations were performed under the orders of the primary physicians.

Inclusion/exclusion criteria

Inclusion criteria included patients diagnosed with PD on the UK Parkinson's Disease Society Brain Bank criteria[16] or PSP based on the Movement Disorder Society (MDS-PSP) diagnostic criteria[17] and native Japanese speakers.

The exclusion criteria included patients with other neurological or psychiatric disorders, patients with unstable general health conditions and patients with a family history suggesting hereditary disease.

Classification of participants

To address the rapid progression of PSP symptoms compared with PD, participants were stratified by age and disease duration. PSP subtypes were classified based on the MDS-PSP criteria into PSP-Richardson's syndrome (PSP-RS), PSP-progressive gait freezing (PSP-PGF), PSP-P and PSP-predominant corticobasal syndrome (PSP-CBS). Due to limited sample sizes, analyses focused on PSP-RS and PSP-PGF subtypes.

Patient characteristics

Data collected included age and gender, education level, disease type and clinical subtype (for PSP), disease duration, Hoehn and Yahr stage for PD, Unified Parkinson's Disease Rating Scale for PD[18] and Progressive Supranuclear Palsy Rating Scale (PSP-RS) for PSP.[19]

Neuropsychological testing

General cognitive function assessment

- Mini-Mental State Examination (MMSE): A cognitive screening tool (cut-off: 24/30 points).[20]
- Hasegawa Dementia Rating Scale-Revised (HDS-R): A widely used tool in Japan (cut-off: 20/30 points).[21]
- Japanese version of the Montreal Cognitive Assessment (MoCA-J): Assesses mild cognitive impairment (cut-off: 26/30 points).[22]

Frontal lobe functional assessment

- Frontal Assessment Battery (FAB): Evaluates executive functions (cut-off: 10/18 points).[23]
- Stroop Color-Word Test: Measures response inhibition and selective attention through reaction time.[24]
- Verbal Fluency Test (phonological): Assesses executive function based on the number of words generated within 1 min.

Attention and working memory assessment

- Trail Making Test (TMT)
  - TMT-A: Assesses selective attention and visual search ability.
  - TMT-B: Evaluates working memory and distributive attention.
  - Completion times were recorded.[25]
- Digit span test (Clinical Assessment for Attention): Assesses attention, working memory and verbal short-term memory.[26]
  - Cut-offs for individuals in their 60s: 5.8 digits (forward) and 4.3 digits (reverse).

Intellectual function assessment

- Raven's Coloured Progressive Matrices (RCPM): Measures visuospatial intellectual function (cut-off: 24/36 points).[27]

Visuospatial function assessment

- Judgement of Line Orientation (Repeatable Battery for the Assessment of Neuropsychological Status): Evaluates visuospatial abilities (total score: 20 points).[28]

Language functional assessment

- Verbal fluency (Meaning) in the HDS-R: This language function assessment measures verbal fluency. The score reflects the number of words (eg, vegetables) generated within 1 min.

Amount of change

For each disease, we compared the results of the first and second neuropsychological tests (MMSE, HDS-R, MoCA-J, RCPM, FAB and TMT) in patients who were retested at least 12 months after the initial test. The amount of change was calculated by subtracting the first test results from the second.

Patient and public involvement

No patient or public involvement was reported.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, V.24.0 for Windows), with a significance threshold of 5% for all tests. Additionally, the χ^2 test was applied to nominal variables.

The statistical methods employed are outlined below:

1. Testing for differences in cognitive dysfunction between the PD and PSP groups.

Basic demographic attributes and neuropsychological test results were compared between the two disease groups using the Student's t-test.

2. Tests of group differences in cognitive dysfunction by clinical subtypes of PD and PSP (PSP-RS and PSP-PGF).

For the three disease subgroups (PD, PSP-RS and PSP-PGF), one-way analysis of variance (ANOVA) was used to compare basic attributes and neuropsychological test scores. Tukey's post hoc test was conducted for multiple comparisons.

3. Trends in cognitive dysfunction by clinical subtype of PD and PSP (PSP-RS and PSP-PGF).

Within each disease group (PD, PSP-RS and PSP-PGF), changes between the first and second neuropsychological tests were analysed using a paired t-test. One-way ANOVA was used to assess changes in test scores across the three groups. Tukey's post hoc test was applied for multiple comparisons. The MoCA-J for PSP-RS was excluded from the analysis due to the small sample size.

RESULTS

Comparison of cognitive dysfunction between PD and PSP

The PD group (n=38) had a mean age of 73.1±6.9 year and a disease duration of 62.7±41.9 months. The PSP group (n=41) had a mean age of 72.9±7.1 year and a disease duration of 57.8±38.5 months, showing no significant differences in age or disease duration between the groups. The comparison of basic attributes and neuropsychological test results for the PD and PSP groups is presented in table 1. Significant differences between the groups were observed in the following measures (the PSP group showed lower scores): MMSE (p=0.001), HDS-R (p=0.001), MoCA-J (p=0.013), RCPM (p=0.039), FAB (p<0.001), verbal fluency (meaning; p<0.001), verbal fluency (phonology; p<0.001), Stroop Color-Word Test (Part I: p=0.020; Part II: p=0.014), Digit Span (backwards: p=0.021), TMT-A (p=0.001), and Line Orientation (p=0.030).

Comparison of cognitive impairment by clinical form of PD and PSP

For the clinical subtypes of PSP, 23 patients were classified as PSP-RS, 14 as PSP-PGF, 3 as PSP-P and 1 as PSP-CBS. All PSP cases met the MDS diagnostic criteria for definite, probable or possible PSP. Four patients were diagnosed with definite PSP-RS, 19 with probable PSP-RS, 1 with definite PSP-PGF, 10 with probable PSP-PGF, 3 with possible PSP-PGF, 3 with probable PSP-P, 1 with possible PSP-CBS and no patients met the criteria for suggestive level. The number of deaths recorded was 5 in the PD group (33 survivors) and 16 in the PSP group (25 survivors). Of the 16 deceased PSP patients, 5 underwent autopsy and were pathologically confirmed as having PSP (either definite PSP-RS or PSP-PGF).

The PSP-RS (n=23) group had a mean age of 72.4±6.3 year and a mean disease duration of 52.0±37.4 months. In comparison, the PSP-PGF group (n=14) had a mean age of 70.6±6.4 year and a mean disease duration of 66.0±40.9 months. No significant differences were observed between the groups in terms of age or disease duration. Furthermore, no significant differences were found in the age and disease duration between the PD and PSP-RS groups or between the PD and PSP-PGF groups. Table 2 provides a comparison of the basic attributes and cognitive function between the PD and PSP clinical subtypes.

The comparison between the PD and PSP-RS groups revealed significant differences in several cognitive measures: MMSE (p<0.001), HDS-R (p<0.001), RCPM (p=0.037), FAB (p=0.001), verbal fluency (semantic; p<0.001), verbal fluency (phonological; p=0.003) and TMT-A (p<0.001). The comparison between the PD and PSP-PGF groups showed a significant difference only in verbal fluency (semantic). Significant differences were also observed between the PSP-RS and PSP-PGF groups in MMSE (p=0.015), HDS-R (p=0.022) and TMT-A (p=0.001), with the PSP-RS group demonstrating significantly lower cognitive function than the PD group. However, there were no significant differences between the PD and PSP-PGF groups, nor between the PSP-RS and PSP-PGF groups in many of the cognitive measures.

Trends in cognitive dysfunction by clinical subtype in PD and PSP

A follow-up cognitive assessment was conducted approximately 12 months after the initial evaluation in 21 (55.2%) patients with PD and 23 (56.1%) patients with PSP, including 11 PSP-RS, 10 PSP-PGF, 1 PSP-P and 1 in PSP-CBS (table 3). The mean follow-up period was 23.6±16.5 months (range: 12–76 months), with the PD group assessed at 28.9±21.2 months and the PSP group at 18.8±8.6 months. By clinical subtypes in PSP, the time to follow-up was 17.4±7.3 months for the PSP-RS group and 21.3±10.2 months for the PSP-PGF group. No significant differences were found between the first and second cognitive function assessments in the PD group. In contrast, the PSP group exhibited significant declines across several cognitive measures, including MMSE (p=0.002),

Table 1 Comparison of basic attributes and cognitive function in PD and PSP groups

Measure	PD (n=38)	PSP (n=41)	P value
Age (years)	73.1±6.9	72.9±7.1	0.899
Gender (male/female)	19/19	26/15	0.229
Education (years)	12.1±2.3	13.6±2.5	0.142
Disease duration (months)	62.7±41.9	57.8±38.5	0.589
Hoehn-Yahr stage	3.1±0.8	—	
UPDRS-III	27.0±12.8	—	
PSP-RS	—	39.1±12.8	
MMSE (total score)	27.4±3.2	23.6±6.1	0.001**
HDS-R (score)	27.1±3.7	23.2±5.1	0.001**
MoCA-J (score)	24.0±4.3	20.2±5.9	0.013*
RCPM (score)	28.2±5.1	25.5±5.8	0.039*
FAB (score)	14.0±2.8	11.0±3.5	<0.001**
Verbal fluency (semantic)	15.6±3.8	9.3±3.8	<0.001**
Verbal fluency (phonological)	11.2±3.7	6.3±3.6	<0.001**
Stroop Color-Word Test			
Part I (s)	22.2±10.4	46.1±39.4	0.020*
Part II (s)	43.3±24.4	75.8±46.3	0.014*
Digit Span (forward)	5.8±1.1	5.1±1.2	0.086
Digit Span (backward)	4.6±1.3	3.5±1.3	0.021*
TMT-A (s)	88.1±37.4	175.3±120.9	0.001**
TMT-B (s)	170.5±135.2	192.4±111.6	0.539
Line Orientation (score)	15.8±2.7	13.0±4.6	0.030*

*p<0.05.
**p<0.01.
FAB, Frontal Assessment Battery; HDS-R, Hasegawa Dementia Rating Scale-Revised; Line Orientation, judgement of Line Orientation in the repeatable battery for the assessment of neuropsychological status; MMSE, Mini-Mental State Examination; MoCA-J, Japanese Version of Montreal Cognitive Assessment; PSP-RS, Progressive Supranuclear Palsy Rating Scale; RCPM, Raven's Coloured Progressive Matrices; TMT, Trail Making Test; UPDRS, Unified Parkinson's Disease Rating Scale.

HDS-R (p=0.004), RCPM (p=0.017), FAB (p<0.001) and TMT-A (p=0.005). When analysing cognitive function by clinical subtype in PSP, the PSP-RS group showed significant declines in MMSE (p=0.019), HDS-R (p=0.005), FAB (p=0.018) and TMT-A (p=0.042), whereas the PSP-PGF group demonstrated significant reductions in MMSE (p=0.010), FAB (p=0.034) and TMT-A (p=0.032).

Additionally, the PD and PSP groups were compared with evaluate changes in cognitive function (table 4). The PSP group demonstrated significantly lower scores than the PD group on the MMSE (p=0.010), HDS-R (p=0.006), FAB (p=0.011) and TMT-A (p=0.011).

Furthermore, we compared the changes in cognitive function between the PD group and the PSP-RS or PSP-PGF group (table 5). The PSP-RS group exhibited a significant decline in MMSE (p=0.006), HDS-R (p=0.001) and FAB (p=0.023) compared with the PD group. The PSP-PGF group showed a significant decline only in FAB (p=0.046) compared with the PD group. No significant differences were observed between the PSP-RS and PSP-PGF groups.

DISCUSSION

Cognitive function in PD and PSP

In this study, PSP showed a more significant decrease in cognitive functions than PD when comparing the two groups. This supports previous research, which found lower scores on the FAB in PSP than in PD.[29] Moreover, patients with PSP demonstrated reduced cognitive abilities, especially in the areas of FAB and verbal fluency compared with PD. The prevalence of early cognitive dysfunction in PSP was higher than in PD, with notable decreases in frontal lobe function and motor IQ[30] than PD and multiple system atrophy (MSA).[15] This study corroborates earlier findings, suggesting that cognitive assessments can be useful in differentiating between PD and PSP.[13]

Cognitive dysfunction in PD results from Lewy body pathology spreading to the limbic system and cortex.[31] In the early stages, it is found in the olfactory bulb and lower brainstem, before spreading to the substantia nigra striatum, with cortical pathology appearing later.[32] In contrast, PSP begins in the frontal lobe, with pathological

Table 2 Comparison of basic attributes and cognitive function in the PD, PSP-RS and PSP-PGF groups

	PD (n=38)	PSP-RS (n=23)	PSP-PGF (n=14)	P value	PD versus RS	PD versus PGF	RS versus PGF
Age (years)	73.1±6.9	72.4±6.3	70.6±6.4	0.502	0.914	0.470	0.721
Gender (male/female)	19/19	15/8	8/6	0.508	0.246	0.647	0.623
Education (years)	12.7±2.3	13.9±2.7	13.8±2.1	0.192	0.224	0.393	0.990
Disease duration (months)	62.7±41.9	52.0±37.4	66.0±40.9	0.505	0.575	0.965	0.568
Hoehn-Yahr stage	3.1±0.8	—	—				
UPDRS-III	27.0±12.8	—	—				
PSP-RS	—	41.8±12.9	32.2±11.2				
MMSE (score)	27.4±3.2	22.1±6.7	26.6±3.6	0.006**	<0.001**	0.846	0.015*
HDS-R (score)	27.1±3.7	22.0±5.6	26.3±3.2	0.004**	<0.001**	0.821	0.022*
MoCA-J (score)	24.0±4.3	19.8±6.7	22.8±3.8	0.063	0.050	0.782	0.349
RCPM (score)	28.2±5.1	24.7±5.4	28.4±5.3	0.033*	0.037*	0.996	0.113
FAB (score)	14.0±2.8	10.8±3.3	12.4±3.2	0.001**	0.001**	0.198	0.311
Verbal fluency (semantic)	15.6±3.8	8.4±4.4	11.1±2.7	<0.001**	<0.001**	0.031**	0.305
Verbal fluency (phonological)	11.2±3.7	5.9±3.7	7.8±3.8	0.004**	0.003**	0.113	0.503
Stroop Color-Word Test							
Part I (s)	22.2±10.5	50.4±43.7	41.9±38.6	0.107	0.085	0.332	0.834
Part II (s)	43.3±24.4	81.7±50.6	64.7±43.8	0.064	0.054	0.426	0.629
Digit Span (forward)	5.8±1.1	5.5±0.9	5.0±1.5	0.246	0.721	0.218	0.638
Digit Span (backward)	4.6±1.3	3.5±0.9	3.7±1.8	0.125	0.135	0.341	0.921
TMT-A (s)	88.1±37.4	212.3±134.7	98.7±39.8	0.006**	<0.001**	0.916	0.001**
TMT-B (s)	170.5±135.2	193.2±98.6	170.6±105.7	0.884	0.879	0.993	0.914
Line Orientation (score)	15.8±2.7	12.7±3.8	15.4±4.1	0.080	0.077	0.957	0.236

*p<0.05.
**p<0.01.
FAB, Frontal Assessment Battery; HDS-R, Hasegawa Dementia Rating Scale-Revised; Line Orientation, judgment of Line Orientation in the repeatable battery for the assessment of neuropsychological status; MMSE, Mini-Mental State Examination; MoCA-J, Japanese Version of Montreal Cognitive Assessment; PD, Parkinson's disease; PSP-PGF, progressive supranuclear palsy-progressive gait freezing; PSP-RS, progressive supranuclear palsy-Richardson's syndrome; PSP-RS, Progressive Supranuclear Palsy Rating Scale; RCPM, Raven's Coloured Progressive Matrices; TMT, Trail Making Test; UPDRS, Unified Parkinson's Disease Rating Scale.

changes spreading to the parietal and temporal lobes via association fibres.[33] Both subcortical (eg, the globus pallidus, midbrain cap and striatum) and cortical (eg, prefrontal and premotor) areas are impaired, resulting in a significant cognitive decrease. Affected areas include the prefrontal cortex, premotor cortex, striatal/thalamic/cortical circuits, midbrain and ascending arousal system.[14] Thus, it was hypothesised that PSP would experience greater cognitive impairment than PD.

Cognitive function by clinical subtype in PD and PSP

Among the three groups—PD, PSP-RS and PSP-PGF—the PSP-RS subtype showed the most significant cognitive decrease, while patients with PD retained the most preserved cognitive function initially. PSP-RS had significantly lower scores on the MMSE, HDS-R and verbal fluency than PD, indicating that cognitive function tests are useful in distinguishing between PD and PSP-RS. However, there were no significant differences between PD and PSP-PGF, except for verbal fluency (meaning). When using cognitive function tests to differentiate PD and PSP, it is crucial to consider the clinical form of PSP.

In comparing PSP-RS and PSP-PGF, significant differences were observed only in MMSE, HDS-R and TMT-A, but PSP-RS consistently showed greater cognitive decrease across all items than PSP-PGF. According to prior studies, cognitive impairment prevalence by PSP clinical subtype was highest in PSP-RS (47.8%), followed by PSP-P (45.5%), PSP-CBS (42.9%) and PSP-PGF (25.0%), with PSP-PGF demonstrating the most preserved cognitive function.[34] No significant differences were found in this study; however, PSP-PGF appeared to maintain better cognitive function overall than PSP-RS, despite the lack of significant differences. PSP-PGF had a larger number of cases than PSP-P in this study because PSP-PGF is more common in Japanese populations.

The larger number of PSP-PGF cases in this study than in previous studies, along with the absence of

Table 3 Cognitive function in PD and PSP groups by clinical form

	PD (n=21)			PSP (n=23)		
	Baseline follow-up		P value	Baseline follow-up		P value
MMSE (score)	27.8±2.7	27.3±2.9	0.370	26.6±4.4	22.7±5.7	0.002**
HDS-R (score)	27.5±2.9	27.4±2.8	0.914	26.7±4.1	23.2±4.1	0.004**
MoCA-J (score)	20.8±2.9	21.3±5.7	0.762	22.0±3.7	21.4±3.8	0.468
RCPM (score)	29.4±4.6	28.4±5.4	0.128	29.2±3.5	26.1±6.0	0.017*
FAB (score)	14.2±2.9	14.3±2.8	0.804	12.5±3.2	10.1±3.1	<0.001**
TMT-A (s)	72.9±35.8	82.8±32.5	0.309	116.2±79.8	208.7±116.6	0.005**
TMT-B (s)	148.1±88.4	173.8±175.2	0.528	160.4±84.9	197.3±106.4	0.092
	RS (n=11)			PGF (n=10)		
	Baseline follow-up		P value	Baseline follow-up		P value
MMSE (score)	25.8±3.3	20.2±6.1	0.019*	28.8±1.2	25.7±3.8	0.010*
HDS-R (score)	27.3±2.2	21.7±4.1	0.005**	28.0±2.3	25.7±3.4	0.094
MoCA-J (score)	—	—	—	24.0±2.0	23.6±2.5	0.808
RCPM (score)	28.8±3.9	25.8±5.8	0.091	29.8±3.5	27.3±6.2	0.238
FAB (score)	11.6±2.3	9.4±2.6	0.018*	13.9±3.4	11.4±3.1	0.034*
TMT-A (s)	155.3±102.1	294.3±102.3	0.042*	70.8±17.1	114.0±44.6	0.032*
TMT-B (s)	143.3±92.2	181.0±103.1	0.162	140.6±56.4	167.3±66.5	0.427

*p<0.05.
**p<0.01.
FAB, Frontal Assessment Battery; HDS-R, Hasegawa Dementia Rating Scale-Revised; MMSE, Mini-Mental State Examination; MoCA-J, Japanese Version of Montreal Cognitive Assessment; PD, Parkinson's disease; PGF, progressive gait freezing; PSP, progressive supranuclear palsy; RCPM, Raven's Coloured Progressive Matrices; RS, Richardson's syndrome; TMT, Trail Making Test.

extensive research on cognitive function across PSP clinical subtypes, is noteworthy.

In verbal fluency tasks, both PSP-RS and PSP-PGF showed significantly lower word counts than PD. Functional MRI studies have demonstrated that both the frontal and temporal lobes play a crucial role in verbal fluency tasks (meaning).[35] PSP has been reported to be more impaired in verbal fluency (phonology) than verbal fluency (meaning).[36] As with prior studies, this research confirmed that verbal fluency (phonology) is more impaired in PSP than in PD. While there was no statistically significant difference in verbal fluency tasks between PSP-RS and PSP-PGF, PSP-RS tended to have lower word counts, highlighting its greater cognitive impairment. Verbal fluency tasks, encompassing phonological and semantic assessments, remain practical tools for differentiating PD from PSP.

Table 4 Comparison of cognitive function changes between the PD and PSP groups

	PD (n=21)	PSP (n=23)	P value
MMSE change	0.5±2.4	3.9±5.4	0.010*
HDS-R change	0.1±2.0	3.3±4.2	0.006**
MoCA-J change	−0.5±3.8	0.6±1.7	0.546
RCPM change	1.0±2.7	3.0±5.0	0.123
FAB change	−0.2±2.7	2.4±2.7	0.003**
TMT-A change	−9.9±36.4	−92.5±96.8	0.011*
TMT-B change	−25.7±153.6	−9.7±107.6	0.771

*p<0.05.
**p<0.01.
FAB, Frontal Assessment Battery; HDS-R, Hasegawa Dementia Rating Scale-Revised; MMSE, Mini-Mental State Examination; MoCA-J, Japanese Version of Montreal Cognitive Assessment; PD, Parkinson's disease; PSP, progressive supranuclear palsy; RCPM, Raven's Coloured Progressive Matrices; TMT, Trail Making Test.

Trends in cognitive function in the PD and PSP items

Over 12 months, the PSP group demonstrated significant cognitive declines, whereas the PD group showed not significant differences in repeated testing. Previous studies corroborate these findings, with dementia prevalence in PSP[30] increasing from 37.5% to 70% after 15 months,[37] while only 18% of patients with PD developed cognitive dysfunction over 7 years.[38] In this study, PSP showed cognitive declines in all tested items except TMT-B and MoCA-J over 12 months, whereas PD exhibited no significant changes in cognitive function. Among the clinical subtypes of PSP, PSP-RS demonstrated declines in MMSE, HDS-R, FAB and TMT-A, while PSP-PGF showed declines in MMSE, FAB and TMT-A. Although both PSP-RS and PSP-PGF exhibited cognitive decline over time, the progression of cognitive impairment in PSP-PGF was slower than that in PSP-RS.

Table 5 Comparison of cognitive function changes between PD, PSP-RS and PSP-PGF groups

	PD (n=21)	PSP-RS (n=11)	PSP-PGF (n=10)	P value	PD versus RS	PD versus PGF	RS versus PGF
MMSE change	0.5±2.4	5.6±6.6	3.1±3.0	0.006**	0.005**	0.219	0.355
HDS-R change	0.1±2.0	5.0±4.1	2.3±3.0	0.001**	<0.001**	0.192	0.160
MoCA-J change	—	—	—	—	—	—	—
RCPM change	1.0±2.7	3.0±4.7	2.5±5.5	0.371	0.402	0.615	0.963
FAB change	−0.2±2.7	2.2±2.6	2.5±3.2	0.023*	0.076	0.046*	0.963
TMT-A change	−9.9±36.4	−139.0±124.9	−43.2±36.0	0.053	0.112	0.190	0.248
TMT-B change	−25.7±153.6	−37.7±30.0	−26.7±75.6	0.712	0.706	1.000	0.760

*p<0.05.
**p<0.01.
FAB, Frontal Assessment Battery; HDS-R, Hasegawa Dementia Rating Scale-Revised; MMSE, Mini-Mental State Examination; MoCA-J, Japanese Version of Montreal Cognitive Assessment; PD, Parkinson's disease; PSP-PGF, progressive supranuclear palsy-progressive gait freezing; RCPM, Raven's Coloured Progressive Matrices; RS, Richardson's syndrome; TMT, Trail Making Test.

Cognitive function was evaluated at intervals of 12 months or longer to better elucidate differences in cognitive function changes between PD and PSP. As this was a retrospective study, the time to re-evaluation varied, as it depended on the timing of patient admission. Ideally, re-evaluation should have been conducted at standardised intervals. The current findings suggest that the observed differences in cognitive function between PD and PSP are significant.

Previous research has reported a higher incidence of cognitive and motor impairment in PSP-RS and PSP-PGF, with PSP-P presenting a comparatively better course.[39] In the present longitudinal study, PSP demonstrated significantly lower cognitive function than PD. However, PSP-PGF exhibited significant differences only in FAB scores compared with PD (p=0.046). Furthermore, no significant differences in longitudinal changes were observed between PSP-RS and PSP-PGF. Given the variability in prognosis among PSP subtypes, increasing the sample size and tracking cognitive changes over time are essential for understanding the clinical course of each subtype.

This study included a larger cohort of PSP-PGF cases than previous studies. Notably, few studies have comprehensively assessed cognitive function in PSP-PGF using multiple neuropsychological tests. The current findings underscore the importance of subtype-specific evaluations of cognitive function in PSP-RS and PSP-PGF.

Limitations

This study has several limitations that must be acknowledged. First, while significant cognitive decline was observed in PSP, the variability among its clinical subtypes posed a challenge. Only PSP-RS and PSP-PGF were included in the analysis. Future research should evaluate cognitive function in other PSP subtypes to provide a more comprehensive understanding of its progression. Second, the study did not include comparisons with MSA, a related disease that shares clinical features with PD and PSP. Third, as a retrospective observational study, this research faced limitations in follow-up consistency. Only 55.2% of PD and 56.1% of patients with PSP underwent re-evaluation, as cognitive assessments were conducted on inpatients admitted for clinical reasons rather than research purposes. This dependence on readmission limited the proportion of cases that could be evaluated a second time. Finally, the retrospective nature of the study introduced inherent constraints, including non-standardised intervals for cognitive reassessment. Ideally, longitudinal studies should employ a prospective design with larger patient cohorts and consistent follow-up periods to elucidate changes in cognitive function more robustly. Despite these limitations, this study highlights important differences in cognitive decline between PSP subtypes and PD, underscoring the need for further investigation.

CONCLUSION

Over 12 months, cognitive impairment progressed significantly in PSP, whereas patients with PD showed no cognitive decline. Among PSP subtypes, PSP-PGF exhibited a slower progression of cognitive impairment than PSP-RS. These findings highlight the need to consider subtype-specific differences in the prognosis of cognitive function when designing treatment and care strategies for patients with PSP.

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ORCID iD

Takeharu Tsuboi http://orcid.org/0009-0008-2899-1615

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